UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/787,844	08/06/2001	Shujath M. Ali	DEX-0176	7509

26259 7590 07/13/2005

LICATLA & TYRRELL P.C.
66 E. MAIN STREET
MARLTON, NJ 08053

EXAMINER	
YU, MISOOK	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 07/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

NEW CENTRAL FAX NUMBER

Effective July 15, 2005

On July 15, 2005, the Central FAX Number will change to **571-273-8300**. This new Central FAX Number is the result of relocating the Central FAX server to the Office's Alexandria, Virginia campus.

Most facsimile-transmitted patent application related correspondence is required to be sent to the Central FAX Number. To give customers time to adjust to the new Central FAX Number, faxes sent to the old number (703-872-9306) will be routed to the new number until September 15, 2005. After September 15, 2005, the old number will no longer be in service and **571-273-8300** will be the only facsimile number recognized for "centralized delivery".

CENTRALIZED DELIVERY POLICY: For patent related correspondence, hand carry deliveries must be made to the Customer Service Window (now located at the Randolph Building, 401 Dulany Street, Alexandria, VA 22314), and facsimile transmissions must be sent to the Central FAX number, unless an exception applies. For example, if the examiner has rejected claims in a regular U.S. patent application, and the reply to the examiner's Office action is desired to be transmitted by facsimile rather than mailed, the reply must be sent to the Central FAX Number.

Office Action Summary	Application No.	Applicant(s)	
	09/787,844	ALI ET AL.	
	Examiner	Art Unit	
	MISOOK YU, Ph.D	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8,9,13-15,17-19 and 21-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8,9,13-15,17-19 and 21-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 3/16/05
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Exhibit A (sequence alignment)*.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/16/2005, and 4/15/2005 has been entered.

Claims 8, 9, 13-15, 17-19, and 21-33 are pending and examined on merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This Office action contains new grounds of objection to the claims.

Claim Objection, Newly Objected

Since claims 13, 17, 21, 22-24, 26, and 27 depend on claim 8 reciting "Pro104" limited to SEQ ID NO: 2, all of the limitations in the rejected dependent claims are the inherent characteristics of SEQ ID NO: 2, thus not further limiting the base claims.

Claim Rejections - 35 USC § 112, Maintained

Claims 8, 9, and 13-15, 17-19, and 21-33 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement for the reason of record. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

This rejection is based on the Office's interpretation of the nature of the invention as drawn to a method of imaging of a gynecologic cancer using an monoclonal or polyclonal antibody which specifically binds to SEQ ID NO: 2 (claims 8, 13), wherein said antibody is labeled (claim 9), or method of delivering a derivatized antibody (the specification at page 7 line 14, appears to limit "derivatized" as attaching cytotoxic agent or other art-known agents to an antibody that binds to SEQ ID NO: 2), which specifically binds to SEQ ID NO:2, to a gynecologic cancer cell in vivo (claims 14, 15, 17), or delivering said derivatized antibody to a gynecologic tumor in vivo (Claims 18, 19, 21), wherein new claims 22-27 characterizes that the protein of the base claims to be protease with active domains, or SEQ ID NO:2, wherein the new claims 28-33 specifies various gynecologic cancer.

Applicant argues that instant Pro104 is same as testisin that are highly expressed in ovarian cancers as disclosed by Tang et al., (2005, Cancer Res., vol. 65, pages 868-78, IDS filed on 03/16/2005), and also as disclosed in Papkoff et al (IDS filed on 03/16/2005).

Applicant's arguments and data shown in the poster presentation of Papkoff et al., and the post-filing publication of Tang et al., have been fully considered, but unpersuasive for the following reasons. First, during the prosecution history, the limitation "Pro104" in the instant claims is determined to be limited to the instant SEQ ID NO: 2 protein. See the Office action mailed on 04/21/2004, and applicant's subsequent response, as well as the interpretation of the claims. The specification as originally filed does not reasonably communicates that the protein known in the art, as "testisin" is

same as the instantly claimed Pro104. The attached sequence alignment aligning the instant SEQ ID NO: 2 against what is the protein known as testisin in the art (Exhibit A) demonstrate that instant SEQ ID NO: 2 is not same as testisin. Therefore, the argument with Tang et al., is not germane to the instantly claimed invention.

As for argument with Papkoff et al., Papkoff et al., discloses the Pro104 is over-expressed in ovarian cancer. However, Papkoff et al., do not establish whether Pro104 is same as the instant SEQ ID NO:2. In fact, one of the figure in the poster, top in the 2nd column appears to indicate that Pro104 in Papkoff et al., is testisin, not instant SEQ ID NO:2. In addition, Papkoff et al., do not establish that whether one could image gynecologic cancers using polyclonal or monoclonal antibody specifically binding to the instant SEQ ID NO:2 encoded by instant SEQ ID NO:1. Papkoff et al., teach that detection of overexpression of Pro104 (testisin) in ovarian cancer tissue samples as compared to normal ovarian tissue.

As stated before in the two previous Office actions, Aloj et al., (2002, Biopolymers. Vol. 66, pages 370-80) teach that in order to target specific molecules inside the body using radiopharmaceuticals such as a radioisotope-labeled antibody, several parameters have to be considered: (1) the target protein should be over-expressed in cancer to be imaged; (2) a radiopharmaceutical should be tested to see whether said radiopharmaceutical specifically binds to the in vivo target *in vivo*; (3) how the unbound radiopharmaceutical is cleared for minimizing unwanted high background (note the abstract, and pages 372-373). The instant specification has failed to teach with a reasonable certainty that the protein encoded by SEQ ID NO:1 is a gynecologic

cancer antigen while the art (see Hooper et al., above) suggests that the protein encoded by SEQ ID NO:1 is a tumor suppressor. Low et al., (1995, Radiology, vol. 195, pages 391-400) also teach that in order to image an ovarian cancer (a species of a gynecologic cancer), selection of an antibody that specially binds to an ovarian cancer-associated antigen, is the first necessary step (see page 391 middle column; the authors selected an antibody targeting Tag-72, a previously known ovarian cancer antigen). Low et al., further teach accuracy of imaging using an antibody directed to a cancer antigen has to be evaluated against other known cancer detection methods such as histology or pathology (note page 393 under the heading "Pathologic Proof", and Table 3 at page 396). Likewise, Krag et al., (1993, Arch. Surg. Vol. 128, pages 819-23) teach method of imaging an ovarian cancer using a radio-labeled (i.e. indium 111-labeled) CYT-103 monoclonal antibody requires selection of an antibody capable of binding to an antigen that is over-expressed in an ovarian cancer (see page 820 under the heading "Patients, Materials, and Methods").

Considering the unpredictable state of art, limited guidance, no examples in the specification how to use the instantly claimed invention, broad breath of the claims, it is concluded that undue experimentation is required to practice the invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D whose telephone number is 571-272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MISOOK YU, Ph.D
Examiner
Art Unit 1642

Form PTO-1449 Modified List of Patents and Publications Cited by Applicant (Use several sheets if necessary) U.S. Department of Commerce	Docket No. DEX-0176	Serial No. 09/787,844
	Applicant Ali and Cafferkey	
	Filing Date August 6, 2001	Group 1642

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

my	CA	Papkoff et al Abstract Number A215 presented on November 18, 2003 at the AACR-NCI-EORTC 2003 International Conference on "Molecular Targets and Cancer Therapeutics discovery, biology and clinical applications".
↓	CB	Tang et al., "Testisin, a Glycosyl-Phosphatidylinositol-Linked Serine Protease, Promotes Malignant Transformation *In vitro* and *In vivo*", Cancer Res. 2005 65(3):868-878

EXAMINER	DATE CONSIDERED
Mousa Y	7-8-05

Exhibit H Page 1 of 2

GenCore version 5.1.6

OM protein - protein search, using sw model

Run on: April 6, 2004, 14:05:54 ; Search time 17 Seconds
(without alignments)
1001.585 Million cell updates/sec

Title: US-09-787-844-2
Perfect score: 1792
Sequence: 1 RRQRGRQAAGEEAMGARGAL.....PSWPLLFPPLLWALPLLGPV 327

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 141681 seqs, 52070155 residues

Total number of hits satisfying chosen parameters: 141681

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : SwissProt_42:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	1728	96.4	314	1	TEST_HUMAN	Q9y6m0 homo sapien
2	1147	64.0	324	1	TEST_MOUSE	Q9jhj7 mus musculu
3	603	33.6	321	1	TRYG_HUMAN	Q9nrr2 homo sapien
4	580	32.4	343	1	PSS8_HUMAN	Q16651 homo sapien
5	574	32.0	290	1	PR27_HUMAN	Q9bqr3 homo sapien
6	562.5	31.4	342	1	PSS8_RAT	Q9es87 rattus norv
7	561.5	31.3	342	1	PSS8_MOUSE	Q9esd1 mus musculu
8	556.5	31.1	311	1	TRYG_MOUSE	Q9qul7 mus musculu
9	544	30.4	273	1	TRYT_SHEEP	Q9xsm2 ovis aries
10	543	30.3	811	1	TMS6_MOUSE	Q9dbi0 mus musculu
11	531.5	29.7	317	1	BSS4_HUMAN	Q9gzn4 homo sapien
12	528.5	29.5	270	1	TRYT_MERUN	P50342 meriones un
13	522	29.1	275	1	TRYT_PIG	Q9n2d1 sus scrofa
14	520	29.0	306	1	BSS4_MOUSE	Q9er10 mus musculu
15	515	28.7	275	1	TRB1_HUMAN	Q15661 homo sapien
16	514.5	28.7	638	1	KAL_MOUSE	P26262 mus musculu
17	514	28.7	275	1	TRB2_HUMAN	P20231 homo sapien
18	513	28.6	638	1	KAL_HUMAN	P03952 homo sapien
19	512	28.6	276	1	MCT6_MOUSE	P21845 mus musculu
20	511	28.5	275	1	TRYT_CANFA	P15944 canis famil
21	511	28.5	638	1	KAL_RAT	P14272 rattus norv
22	509.5	28.4	273	1	MCT7_RAT	P27435 rattus norv
23	509	28.4	811	1	TMS6_HUMAN	Q8iu80 homo sapien
24	508.5	28.4	454	1	TMS3_HUMAN	P57727 homo sapien
25	507	28.3	273	1	MCT7_MOUSE	Q02844 mus musculu
26	505	28.2	453	1	TMS3_MOUSE	Q8k1t0 mus musculu
27	500	27.9	274	1	MCT6_RAT	P50343 rattus norv
28	499	27.8	275	1	TRYA_HUMAN	P15157 homo sapien
29	490.5	27.4	435	1	TMS4_MOUSE	Q8vca5 mus musculu
30	489.5	27.3	418	1	HATT_HUMAN	O60235 homo sapien
31	487.5	27.2	455	1	TMS5_MOUSE	Q9er04 mus musculu
32	483.5	27.0	625	1	FA11_HUMAN	P03951 homo sapien
33	478	26.7	437	1	TMS4_HUMAN	Q9nrs4 homo sapien
34	477.5	26.6	417	1	HEPS_HUMAN	P05981 homo sapien
35	472.5	26.4	422	1	DES1_HUMAN	Q9u152 homo sapien
36	468	26.1	490	1	TMS2_MOUSE	Q9jiq8 mus musculu
37	466	26.0	436	1	HEPS_MOUSE	O35453 mus musculu
38	459.5	25.6	492	1	TMS2_HUMAN	O15393 homo sapien
39	457.5	25.5	457	1	TMS5_HUMAN	Q9h3e3 homo sapien
40	455.5	25.4	415	1	ACRO_PIG	P08001 sus scrofa
41	455.5	25.4	810	1	PLMN_HUMAN	P00747 homo sapien
42	454.5	25.4	1069	1	ENTK_MOUSE	P97435 mus musculu
43	454	25.3	338	1	PLMN_HORSE	P80010 equus cabal
44	452.5	25.3	436	1	ACRO_MOUSE	P23578 mus musculu
45	447	24.9	416	1	HEPS_RAT	Q05511 rattus norv

ALIGNMENTS

RESULT 1
TEST_HUMAN
ID TEST_HUMAN STANDARD; PRT; 314 AA.
AC Q9Y6M0; Q9NS34; Q9P2V6;
DT 16-OCT-2001 (Rel. 40, Created)
DT 16-OCT-2001 (Rel. 40, Last sequence update)
DT 15-MAR-2004 (Rel. 43, Last annotation update)
DE Testisin precursor (EC 3.4.21.-) (Eosinophil serine protease 1) (ESP-
DE 1) (UNQ266/PRO303).
GN PRSS21 OR TEST1 OR ESP1.
OS Homo sapiens (Human).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OX NCBI_TaxID=9606;
RN [1]
RP SEQUENCE FROM N.A. (ISOFORM 1).
RC TISSUE=Eosinophil;
RX MEDLINE=99045401; PubMed=9826525;
RA Inoue M., Kanbe N., Kurosawa M., Kido H.;
RT "Cloning and tissue distribution of a novel serine protease esp-1 from
RT human eosinophils.";
RL Biochem. Biophys. Res. Commun. 252:307-312(1998).
RN [2]
RP SEQUENCE FROM N.A. (ISOFORM 3).
RX MEDLINE=20068805; PubMed=10600542;
RA Inoue M., Isobe M., Itoyama T., Kido H.;
RT "Structural analysis of esp-1 gene (PRSS 21).";
RL Biochem. Biophys. Res. Commun. 266:564-568(1999).
RN [3]
RP SEQUENCE FROM N.A. (ISOFORMS 1 AND 2).
RC TISSUE=Cervical carcinoma;
RX MEDLINE=99323395; PubMed=10397266;
RA Hooper J.D., Nicol D.L., Dickinson J.L., Eyre H.J., Scarman A.L.,
RA Normyle J.F., Stuttgen M.A., Douglas M.L., Loveland K.A.,
RA Sutherland G.R., Antalis T.M.;
RT "Testisin, a new human serine proteinase expressed by premeiotic
RT testicular germ cells and lost in testicular germ cell tumors.";
RL Cancer Res. 59:3199-3205(1999).
RN [4]
RP SEQUENCE FROM N.A.
RX MEDLINE=20461760; PubMed=11004480;
RA Hooper J.D., Bowen N., Marshall H., Cullen L.M., Sood R., Daniels R.,
RA Stuttgen M.A., Normyle J.F., Higgs D.R., Kastner D.L., Ogbourne S.M.,
RA Pera M.F., Jazwinska E.C., Antalis T.M.;
RT "Localization, expression and genomic structure of the gene encoding
RT the human serine protease testisin.";
RL Biochim. Biophys. Acta 1492:63-71(2000).
RN [5]
RP SEQUENCE FROM N.A. (ISOFORM 1).
RX MEDLINE=22887296; PubMed=12975309;
RA Clark H.F., Gurney A.L., Abaya E., Baker K., Baldwin D., Brush J.,
RA Chen J., Chow B., Chui C., Crowley C., Currell B., Deuel B., Dowd P.,
RA Eaton D., Foster J., Grimaldi C., Gu Q., Hass P.E., Heldens S.,
RA Huang A., Kim H.S., Klimowski L., Jin Y., Johnson S., Lee J.,
RA Lewis L., Liao D., Mark M., Robbie E., Sanchez C., Schoenfeld J.,
RA Seshagiri S., Simmons L., Singh J., Smith V., Stinson J., Vagts A.,

```
RA   Vandlen R., Watanabe C., Wieand D., Woods K., Xie M.-H., Yansura D.,
RA   Yi S., Yu G., Yuan J., Zhang M., Zhang Z., Goddard A., Wood W.I.,
RA   Godowski P.;
RT   "The secreted protein discovery initiative (SPDI), a large-scale
RT   effort to identify novel human secreted and transmembrane proteins: a
RT   bioinformatics assessment.";
RL   Genome Res. 13:2265-2270(2003).
CC   -!- FUNCTION: Could regulate proteolytic events associated with
CC       testicular germ cell maturation.
CC   -!- SUBCELLULAR LOCATION: Attached to the membrane by a GPI-anchor
CC       (Potential).
CC   -!- ALTERNATIVE PRODUCTS:
CC       Event=Alternative splicing; Named isoforms=3;
CC       Name=1; Synonyms=L;
CC         IsoId=Q9Y6M0-1; Sequence=Displayed;
CC       Name=2; Synonyms=S;
CC         IsoId=Q9Y6M0-2; Sequence=VSP_005389;
CC       Name=3;
CC         IsoId=Q9Y6M0-3; Sequence=VSP_005390;
CC   -!- TISSUE SPECIFICITY: Expressed predominantly in premeiotic
CC       testicular germ cells, mostly late pachytene and diplotene
CC       spermatocytes.
CC   -!- SIMILARITY: Belongs to peptidase family S1.
CC   ---------------------------------------------------------------------
CC   This SWISS-PROT entry is copyright. It is produced through a collaboration
CC   between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC   the European Bioinformatics Institute. There are no restrictions on its
CC   use by non-profit institutions as long as its content is in no way
CC   modified and this statement is not removed. Usage by and for commercial
CC   entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC   or send an email to license@isb-sib.ch).
CC   ---------------------------------------------------------------------
DR   EMBL; AF058300; AAD41588.1; -.
DR   EMBL; AB031329; BAA83520.1; -.
DR   EMBL; AB031330; BAA83521.1; -.
DR   EMBL; AB031331; BAA89532.1; -.
DR   EMBL; AF058301; AAF79019.1; -.
DR   EMBL; AF058301; AAF79020.1; -.
DR   EMBL; AY359034; AAQ89393.1; -.
DR   HSSP; P00763; 1DPO.
DR   MEROPS; S01.011; -.
DR   Genew; HGNC:9485; PRSS21.
DR   MIM; 608159; -.
DR   GO; GO:0005737; C:cytoplasm; TAS.
DR   GO; GO:0005624; C:membrane fraction; TAS.
DR   GO; GO:0005886; C:plasma membrane; TAS.
DR   GO; GO:0008236; F:serine-type peptidase activity; TAS.
DR   InterPro; IPR009003; Cys_Ser_trypsin.
DR   InterPro; IPR001254; Peptidase_S1.
DR   InterPro; IPR001314; Peptidase_S1A.
DR   Pfam; PF00089; trypsin; 1.
DR   PRINTS; PR00722; CHYMOTRYPSIN.
DR   SMART; SM00020; Tryp_SPc; 1.
DR   PROSITE; PS50240; TRYPSIN_DOM; 1.
DR   PROSITE; PS00134; TRYPSIN_HIS; 1.
DR   PROSITE; PS00135; TRYPSIN_SER; 1.
KW   Hydrolase; Serine protease; Glycoprotein; Signal; GPI-anchor; Zymogen;
KW   Alternative splicing; Lipoprotein.
FT   SIGNAL       1     19       POTENTIAL.
FT   PROPEP      20     41       POTENTIAL.
FT   CHAIN       42    288       TESTISIN.
FT   PROPEP     289    314       REMOVED IN MATURE FORM (POTENTIAL).
FT   ACT_SITE    82     82       CHARGE RELAY SYSTEM (POTENTIAL).
FT   ACT_SITE   137    137       CHARGE RELAY SYSTEM (POTENTIAL).
FT   ACT_SITE   238    238       CHARGE RELAY SYSTEM (POTENTIAL).
FT   DISULFID    33    157       POTENTIAL.
FT   DISULFID    67     83       POTENTIAL.
FT   DISULFID   171    244       POTENTIAL.
FT   DISULFID   204    223       POTENTIAL.
FT   DISULFID   234    262       POTENTIAL.
FT   LIPID      288    288       GPI-anchor amidated serine (Potential).
FT   CARBOHYD   167    167       N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD   200    200       N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD   273    273       N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   VARSPLIC    87     88       Missing (in isoform 2).
FT                               /FTId=VSP_005389.
FT   VARSPLIC   222    235       Missing (in isoform 3).
FT                               /FTId=VSP_005390.
SQ   SEQUENCE   314 AA;  34884 MW;  E738CF73F6B56B98 CRC64;

  Query Match             96.4%;  Score 1728;  DB 1;  Length 314;
  Best Local Similarity   100.0%;  Pred. No. 1.2e-147;
  Matches  314;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy         14 MGARGALLLALLLARAGLRKPESQEAAPLSGPCGRRVITSRIVGGEDAELGRWPWQGSLR 73
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MGARGALLLALLLARAGLRKPESQEAAPLSGPCGRRVITSRIVGGEDAELGRWPWQGSLR 60

Qy         74 LWDSHVCGVSLLSHRWALTAAHCFETYSDLSDPSGWMVQFGQLTSMPSFWSLQAYYTRYF 133
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 LWDSHVCGVSLLSHRWALTAAHCFETYSDLSDPSGWMVQFGQLTSMPSFWSLQAYYTRYF 120

Qy        134 VSNIYLSPRYLGNSPYDIALVKLSAPVTYTKHIQPICLQASTFEFENRTDCWVTGWGYIK 193
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 VSNIYLSPRYLGNSPYDIALVKLSAPVTYTKHIQPICLQASTFEFENRTDCWVTGWGYIK 180

Qy        194 EDEALPSPHTLQEVQVAIINNSMCNHLFLKYSFRKDIFGDMVCAGNAQGGKDACFGDSGG 253
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 EDEALPSPHTLQEVQVAIINNSMCNHLFLKYSFRKDIFGDMVCAGNAQGGKDACFGDSGG 240

Qy        254 PLACNKNGLWYQIGVVSWGVGCGRPNRPGVYTNISHHFEWIQKLMAQSGMSQPDPSWPLL 313
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 PLACNKNGLWYQIGVVSWGVGCGRPNRPGVYTNISHHFEWIQKLMAQSGMSQPDPSWPLL 300

Qy        314 FFPLLWALPLLGPV 327
              ||||||||||||||
Db        301 FFPLLWALPLLGPV 314
```

```
RESULT 2
TEST_MOUSE
ID   TEST_MOUSE     STANDARD;      PRT;   324 AA.
AC   Q9JHJ7; Q9DA14;
DT   16-OCT-2001 (Rel. 40, Created)
DT   16-OCT-2001 (Rel. 40, Last sequence update)
DT   15-MAR-2004 (Rel. 43, Last annotation update)
DE   Testisin precursor (EC 3.4.21.-) (Tryptase 4).
GN   PRSS21.
OS   Mus musculus (Mouse).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
OX   NCBI_TaxID=10090;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   STRAIN=129/Sv;
RX   MEDLINE=21153229; PubMed=11231276;
RA   Scarman A.L., Hooper J.D., Roucaut K.J., Sit M.-L., Webb G.C.,
RA   Normyle J.F., Antalis T.M.;
RT   "Organization and chromosomal localization of the murine Testisin gene
RT   encoding a serine protease temporally expressed during
RT   spermatogenesis.";
RL   Eur. J. Biochem. 268:1250-1258(2001).
RN   [2]
RP   SEQUENCE FROM N.A.
RC   STRAIN=BALB/c; TISSUE=Testis;
RX   PubMed=11259427;
RA   Wong G.W., Li L., Madhusudhan M.S., Krilis S.A., Gurish M.F.,
RA   Rothenberg M.E., Sali A., Stevens R.L.;
RT   "Tryptase 4, a new member of the chromosome 17 family of mouse serine
RT   proteases.";
RL   J. Biol. Chem. 276:20648-20658(2001).
RN   [3]
RP   SEQUENCE OF 3-324 FROM N.A.
RC   STRAIN=C57BL/6J; TISSUE=Testis;
RX   MEDLINE=21085660; PubMed=11217851;
RA   Kawai J., Shinagawa A., Shibata K., Yoshino M., Itoh M., Ishii Y.,
```

Organization TC1600 Bldg./Room REMSEN

U. S. DEPARTMENT OF COMMERCE
COMMISSIONER FOR PATENTS
P.O. BOX 1450
ALEXANDRIA, VA 22313-1450
IF UNDELIVERABLE RETURN IN TEN DAYS

OFFICIAL BUSINESS

UNITED STATES PO
02 1A
00042044
MAILED FR

AN EQUAL OPPORTUNITY EMPLOYER

IA

A ☒ INSUFFICIENT ADDRESS
C ☐ ATTEMPTED NOT KNOWN
S ☐ NO SUCH NUMBER/ STREET
☐ NOT DELIVERABLE AS ADDRESSED - UNABLE TO FORWARD
☐ OTHER

RTS
RETURN TO SENDER

RECEIVED
JUL 22 2005
USPTO MAIL CENTER